(FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 16:07:05 ON 09 AUG 2001)
DEL HIS
L1 459784 S DEHYDROGENASE?
L2 50093 S L1 AND ALCOHOL
L3 14 S L1 AND (ALCOHOL HYDROGENASE?)
L4 14 DUP REM L3 (0 DUPLICATES REMOVED)
L5 14 SORT L4 PY

FILE 'STNGUIDE' ENTERED AT 16:20:23 ON 09 AUG 2001

=> d an ti so au ab pi l5 2 4 7 9
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS, BIOSIS' - CONTINUE? (Y)/N:y

L5 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2001 ACS
AN 1972:484806 CAPLUS
DN 77:84806
TI Evolution of enzymes
SO Enzymes, 3rd Ed. (1970), Volume 1, 267-339. Editor(s): Boyer, Paul D. Publisher: Academic, New York, N. Y.
CODEN: 25GLAS
AU Smith, Emil L.
AB A review. Much of the amino acid terminal sequence in **alc. hydrogenase** (I) is similar to that of glyceraldehyde-3-phosphate **dehydrogenase** (II). Probably I and II differentiated by gene duplication very early in evolution. Prepns. of cytochrome c isolated from the hearts of 16 persons of European, Asiatic, and African origin showed the same chymotryptic peptide pattern and had identical amino acid compn. 243 refs.

L5 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1977:248984 BIOSIS
TI HYDROLYSIS AND ISOMERIZATION OF TRANS-TRANS FARNESYL DI PHOSPHATE BY ANDROGRAPHIS TISSUE CULTURE ENZYMES.
SO EUR J BIOCHEM, (1977) 77 (1), 101-106.
CODEN: EJBCAI. ISSN: 0014-2956.
AU MACKIE H; OVERTON K H
AB Incubation of (3R,5S)-[5-3H1]mevalonate + (3RS)-[2-14C]mevalonate with Andrographis cell-free extract leads to trans,trans-farnesol and cis,trans-farnesol which both totally retain tritium. This conflicts with our previous results which predict 1/3 tritium loss in the cis,trans-farnesol. Inversion at C-1 during hydrolysis of trans,trans-farnesyl diphosphate to trans,trans-farnesol could explain this anomaly. (1S)-trans, trans-[1,3H1]Farnesyl diphosphate and phosphate and (1R)-trans,trans-[1-3H1]-farnesyl diphosphate and phosphate, all prepared chemically, were hydrolyzed with Andrographis phosphatase, and alkaline phosphatase and hydrogenolyzed with lithium aluminium hydride and the product alcohols exchanged with [horse] liver **alcohol hydrogenase** [EC 1.1.1.1]. Both Andrographis phosphatase and [calf-intestinal] alkaline phosphatase [EC 3.1.3.1] hydrolyze trans,trans-farnesyl diphosphate and trans,trans-farnesyl phosphate with retention. Hydrolysis of trans,trans[1-18O]farnesyl diphosphate in H218O with both phosphatases supports P-O fission. The C-1 configuration in (1S)-trans,trans-[1-3H1]farnesyl diphosphate and phosphate and (1R)-trans,trans-[1-3H1]farnesyl diphosphate and phosphate is progressively racemized in 0.01 M NH4OH/MeOH (1/9) at -20.degree. C.

L5 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2001 ACS
AN 1981:528318 CAPLUS
DN 95:128318
TI 5-Methylnicotinamide-adenine dinucleotide. Kinetic investigation with major and minor isoenzymes of liver alcohol **dehydrogenase** and structural determination of its binary complex with alcohol **dehydrogenase**

SO Eur. J. Biochem. (1981), 118(3), 479-86
CODEN: EJBCAI; ISSN: 0014-2956
AU Samama, Jean Pierre; Wrixon, Anthony D.; Biellmann, Jean Francois
AB 5-Methyl-NAD (I) and 3-cyano-5-methylpyridine adenine dinucleotide were prepd. from 5-methylthio-NAD (II) by chem. conversion. II was obtained by enzymic transglucosidation. Model compds. ascertained the structure. None of the dinucleotides methylated at C-5 was active with the major isoenzyme EE of horse liver alc. **dehydrogenase**, but activity with I was measured with the minor isoenzymes. The binding of I to liver alc. **dehydrogenase**, investigated by x-ray diffraction methods to 0.37-nm resoln., occurs with the pyridinium ring away from the active site as previously described for 3-iodopyridine adenine and pyridine adenine dinucleotides. A general conclusion on the use of inhibitors as tools for exploration of the active site is drawn.

L5 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2001 ACS
AN 1987:403203 CAPLUS
DN 107:3203
TI Characterization of a transient intermediate formed in the liver alcohol **dehydrogenase**-catalyzed reduction of 3-hydroxy-4-nitrobenzaldehyde
SO Biochemistry (1987), 26(11), 3058-67
CODEN: BICHAW; ISSN: 0006-2960
AU MacGibbon, Alastair K. H.; Koerber, Steven C.; Pease, Kathleen; Dunn, Michael F.
AB The compds. 3-hydroxy-4-nitrobenzaldehyde and 3-hydroxy-4-nitrobenzyl alc. are introduced as new chromophoric substrates for probing the catalytic mechanism of horse liver alc. **dehydrogenase** (LADH). Ionization of the phenolic OH group shifts the spectrum of the aldehyde from 360 to 433 nm (pKa = 6.0), whereas the spectrum of the alc. shifts from 350 to 417 nm (pKa = 6.9). Rapid-scanning, stopped-flow (RSSF) studies at alk. pH show that the LADH-catalyzed interconversion of these compds. occurs via the formation of an enzyme-bound intermediate with a blue-shifted spectrum. When reaction is limited to a single turnover of enzyme sites, the formation and decay of the intermediate when aldehyde reacts with enzyme-bound NADH [E(NADH)] are characterized by 2 relaxations (.lambda.f - 3.lambda.s). Detailed stopped-flow kinetic studies were carried out to investigate the disappearance of aldehyde and NADH, the formation and decay of the intermediate, the displacement of Auramine O by substrate, and 2H kinetic isotope effects. NADH oxidn. takes place at the rate of the slower relaxation (.lambda.s). When NADD is substituted for NADH, .lambda.s is subject to a small primary isotope effect (.lambda.sH.lambda.sD = 2.0). The events that occur in .lambda.s precede .lambda.f. These findings identify the intermediate as a ternary complex contg. bound NAD and some form of 3-hydroxy-4-nitrobenzyl alc. The blue-shifted spectrum of the intermediate strongly implies a structure wherein the phenolic OH is neutral. When constrained to a mechanism that assumes only the neutral phenolic form of the substrate binds and reacts and that the intermediate is an E(NAD, product) complex, computer simulations yield RSSF and single-wavelength time courses that are qual. and semiquant. consistent with the exptl. data. It is concluded that the LADH substrate site can be divided into 2 subsites: a highly polar, electropos. subsite in the vicinity of the active site Zn and, just a few angstroms away, a rather nonpolar region. The polar subsite promotes formation of the 2 interconverting reactive ternary complexes. The nonpolar region is the binding site for the hydrocarbon-like side chains of substrates and, in the case of 3-hydroxy-4-nitrobenzaldehyde, conveys specificity for the neutral form of the phenolic group.

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Novartis Found Symp 1998;216:19-24; discussion 24-34

Metabolic consequences of alcohol ingestion.

Peters TJ, Preedy VR

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Many of the pathophysiological effects of alcohol ingestion relate to the pathways of ethanol metabolism. However, some of the acute and chronic effects of ethanol use are also attributable to the direct effects of ethanol, e.g. on membrane fluidity. Oxidation of ethanol to acetaldehyde is catalysed by alcohol dehydrogenase (ADH). There are at least six classes of ADH, some of which show inter-individual variation, i.e. genetic polymorphism, that influences the rate of ethanol oxidation. A consequence of ethanol oxidation is an increase in the NADH/NAD redox potential within the cytosol and mitochondria with subsequent alteration in several tissue metabolites. The popular hypothesis that most, if not all, of the consequences of chronic alcohol ingestion can be explained by these redox changes is still unproven. This should be considered in the context that most metabolic pathways of the liver are affected by alcohol, as are several endocrine axes in the whole body. In fact most, if not all, tissues and organs are deleteriously affected by chronic ingestion. Acetaldehyde, the product of ethanol oxidation, is chemically highly reactive, toxic and immunogenic. However, the concentrations achieved in vivo usually fall short of those used to produce these toxic effects in experimental situations. Oxidation of acetaldehyde is also coupled to redox changes, although primarily affecting the intra-mitochondrial redox. In addition, further oxidative pathways of ethanol metabolism can lead to the formation of fatty acid ethyl esters, hydroxyethyl free radicals and reactive oxygen species via the ethanol-specific cytochrome P450-2E1 system. There is no conclusive evidence that nutrient supplementation has beneficial effects on overall ethanol-mediated tissue damage.

Publication Types:

- Review
- Review, tutorial

PMID: 9949785, UI: 99134944

Prog Nucleic Acid Res Mol Biol 2000;64:295-341

Regulation of the mammalian alcohol dehydrogenase genes.

Edenberg HJ

Department of Biochemistry, Indiana University School of Medicine, Indianapolis 46202, USA.

This review focuses on the regulation of the mammalian medium-chain alcohol dehydrogenase (ADH) genes. This family of genes encodes enzymes involved in the reversible oxidation of alcohols to aldehydes. Interest in these enzymes is increased because of their role in the metabolism of beverage alcohol as well as retinol, and their influence on the risk for alcoholism. There are six known classes ADH genes that evolved from a common ancestor. ADH genes differ in their patterns of expression: most are expressed in overlapping tissue-specific patterns, but class III ADH genes are expressed ubiquitously. All have proximal promoters with multiple cis-acting elements. These elements, and the transcription factors that can interact with them, are being defined. Subtle differences in sequence can affect affinity for these factors, and thereby influence the expression of the genes. This provides an interesting system in which to examine the evolution of tissue specificity. Among transcription factors that are important in multiple members of this gene family are the C/EBPs, Sp1,USF, and AP1, HNF-1, CTF/NF-1, glucocorticoid, and retinoic acid receptors, and several as-yet unidentified negative elements, are important in at least one of the genes. There is evidence that cis-acting elements located far from the proximal promoter are necessary for proper expression. Three of the genes have upstream AUGs in the 5' nontranslated regions of their mRNA, unusual for mammalian genes. The upstream AUGs have been shown to significantly affect expression of the human ADH5 gene.

Publication Types:

- Review
- Review, academic

PMID: 10697413, UI: 20162515

Pharmacology 2000 Sep;61(3):184-91

Pharmacogenetics of the alcohol dehydrogenase system.

Jornvall H, Hoog JO, Persson B, Pares X

Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden.

Alcohol dehydrogenase (ADH) constitutes a complex enzyme system with different forms and extensive multiplicity. A combination of constant and variable properties regarding function, multiplicity and structure of ADH is highlighted for the human system and extended to ADH forms in general. Future perspectives suggest continued studies in specific directions for distinction of metabolic, regulatory and pharmacogenetic roles of ADH. Copyright 2000 S. Karger AG, Basel

Publication Types:

- Review
- Review, tutorial

PMID: 10971204, UI: 20429316

FEBS Lett 2000 Dec 1;486(1):49-51

Main ethanol metabolizing alcohol dehydrogenases (ADH I and ADH IV): biochemical functions and the physiological manifestation.

Ashmarin IP, Danilova RA, Obukhova MF, Moskvitina TA, Prosorovsky VN

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ashmarin@3.human.bio.msu.ru

The range of the biochemical reactions which can be catalyzed by ADH I and ADH IV is extremely wide. The most characterized functions of these enzymes are protection against excess endogenous acetaldehyde, products of lipid peroxidation, exogenous alcohols and some xenobiotics. It was found also that ADH I and ADH IV are important members of the enzyme system synthesizing retinoic acid (especially during embryogenesis). They can oxidize some steroids and participate in bioamine and prostaglandin metabolism but so far the extent of their contribution to the latter processes is under discussion. Recent data suggest a correlation between the activity of ADH I in some organs and fine physiological processes including behavior regulation and craving for alcohol in albino rats.

Publication Types:

- Review
- Review, tutorial

PMID: 11108841, UI: 20562799

Chem Biol Interact 2001 Jan 30;130-132(1-3):699-705

Forms and functions of human SDR enzymes.

Oppermann UC, Filling C, Jornvall H

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Short-chain dehydrogenases/reductases (SDR) are defined by distinct, common sequence motifs but constitute a functionally heterogenous superfamily of enzymes. At present, well over 1600 members from all forms of life are annotated in databases. Using the defined sequence motifs as queries, 37 distinct human members of the SDR family can be retrieved. The functional assignments of these forms fall minimally into three main groups, enzymes involved in intermediary metabolism, enzymes participating in lipid hormone and mediator metabolism, and open reading frames (ORFs) of yet undeciphered function. This overview, prepared just before completion of the human genome project, gives the different human SDR forms and relates them to human diseases.

Publication Types:

- Review
- Review, tutorial

PMID: 11306087, UI: 21203497

Chem Biol Interact 2001 Jan 30;130-132(1-3):469-80

Genetic dissection of retinoid dehydrogenases.

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Biochemical studies indicate that alcohol dehydrogenase (ADH) metabolizes retinol to retinal, and that aldehyde dehydrogenase (ALDH) metabolizes retinal to retinoic acid, a molecule essential for growth and development. Summarized herein are several genetic studies supporting in vivo functions for ADH and ALDH in retinoic acid synthesis. Gene targeting was used to create knockout mice for either Adh1 or Adh4. Both knockout mice were viable and fertile without obvious defects. However, when wild-type and Adh4 knockout mice were subjected to vitamin A deficiency during gestation, the survival rate at birth was 3.3-fold lower for Adh4 knockout mice. When adult mice were examined for production of retinoic acid following retinol administration, Adh1 knockout mice exhibited 10-fold lower retinoic acid levels in liver compared with wild-type, whereas Adh4 knockout mice differed from wild-type by less than 2-fold. Thus, Adh1 plays a major role in the metabolism of a large dose of retinol to retinoic acid in adults, whereas Adh4 plays a role in maintaining sufficient retinol metabolism for development during retinol deficiency. ALDHs were examined by overexpression studies in frog embryos. Injection of mRNAs for either mouse Raldh1 or Raldh2 stimulated retinoic acid synthesis in frog embryos at the blastula stage when retinoic acid is normally undetectable. Overexpression of human ALDH2, human ALDH3, and mouse Aldh-pb did not stimulate retinoic acid production. In addition, Raldh2 knockout mice exhibit embryonic lethality with defects in retinoid-dependent tissues. Overall, these studies provide genetic evidence that Adh1, Adh4, Raldh1, and Raldh2 encode retinoid dehydrogenases involved in retinoic acid synthesis in vivo.

Publication Types:

- Review
- Review, tutorial

PMID: 11306068, UI: 21203478

1: EXS 1994;71:279-90 Related Articles, Books

Retinoids and the alcohol dehydrogenase gene family.

Duester G.

La Jolla Cancer Research Foundation, California 92037.

Alcohol dehydrogenase (ADH) is best known as the enzyme which catalyzes the reversible oxidation/reduction of ethanol/acetaldehyde. However, mammalian ADH has also been shown to function in vitro as a retinol dehydrogenase in the conversion of retinol (vitamin A alcohol) to retinoic acid, a hormone which regulates gene expression at the transcriptional level. It is clear that retinol must be converted to more active retinoid forms in order to fulfill its roles in growth, development, and cellular differentiation. An important unsolved issue in retinoid research is the control of retinoic acid synthesis from retinol during differentiation. Several enzymes which participate in the conversion of retinol to retinoic acid in vitro have been isolated, but more information on their relative importance is needed. Human ADH exists as a family of isozymes encoded by seven genes which are differentially expressed in adult and fetal mammalian tissues, being found preferentially in the epithelial cells which are known to synthesize and respond to retinoic acid. Retinoic acid is also known to play a role in neural tube development in vertebrate embryos. Excessive doses of retinoic acid or ethanol are both teratogenic for neural tube development. A relationship may exist between these two types of teratogenesis due to the role of ADH in both retinol and ethanol metabolism and the ability of ethanol to competitively inhibit retinol oxidation. There is a lack of information on the expression patterns of ADH genes in early embryos, but transgenic mouse studies are presented here which show that the human ADH3 gene can be expressed in several mouse embryonic tissues including the neural tube. Thus, ethanol-induced neural tube defects seen in cases of fetal alcohol syndrome may be due to ethanol inhibition of retinol oxidation catalyzed by an embryonic ADH. This could potentially lower retinoic acid levels in the neural tube to the extent that gene expression is not properly regulated, resulting in morphological defects.

PMID: 8032159 [PubMed - indexed for MEDLINE]

European Journal of Biochemistry, Vol 118, 479-486, Copyright © 1981 by Federation of European Biochemical Societies

ARTICLES

5-Methylnicotinamide-adenine dinucleotide. Kinetic investigation with major and minor isoenzymes of liver alcohol dehydrogenase and structural determination of its binary complex with alcohol dehydrogenase

JP Samama, AD Wrixon and JF Biellmann

5-Methylnicotinamide-adenine dinucleotide and 3-cyano-5-methylpyridine- adenine dinucleotide was prepared from 5-methylthionicotinamide-adenine dinucleotide by chemical conversion. The 5-methylthionicotinamide- adenine dinucleotide was obtained by enzymic transglucosidation. Model compounds ascertained the structure. None of the dinucleotides methylated at C-5 was active with the major isoenzyme EE of horse liver alcohol dehydrogenase, but activity with 5-methylnicotinamide-adenine dinucleotide was measured with the minor isoenzymes. The binding of 5-methylnicotinamide-adenine dinucleotide to liver alcohol dehydrogenase, investigated by X-ray diffraction methods to 0.37-nm resolution, occurs with the pyridinium ring away from the active site as previously described for 3-iodopyridine-adenine and pyridine-adenine dinucleotides. A general conclusion on the use of inhibitors as tools for exploration of the active site is drawn.